

## **AMENDMENT**

### **IN THE CLAIMS**

Please cancel the presently pending claims, which include those up to claim 84, and add new claims 85-203, as follows:

85. (new) A transfection agent comprising a peptide of between about 16 to 30 amino acid residues, said peptide comprising:

- a) a hydrophobic domain comprising at least four amino acid residues, wherein the hydrophobic domain comprises a plurality of aromatic amino acid residues and a first hydrophobic locus spaced by at least one amino acid residue from a second hydrophobic locus, wherein each of the first and second hydrophobic loci comprise one or more hydrophobic amino acid residues independently selected from the group consisting of Phe, Tyr, Trp, Thr, Met, Leu, Val, Ile, Ala, and His, and wherein at least two of said plurality of aromatic amino acid residues occur in a pair in the first hydrophobic locus or the second hydrophobic locus;
- b) a hydrophilic domain comprising up to about twelve amino acid residues, wherein the hydrophilic domain comprises a plurality of basic amino acid residues;
- c) optionally a spacer sequence between said hydrophobic and said hydrophilic domain, wherein said spacer comprises from between one to about ten amino acid residues; and
- d) further optionally a functional group conjugated to one or more termini of said peptide.

86. (new) A transfection agent according to claim 85 wherein said hydrophilic domain is a cation-rich sequence comprised of at least two lysine residues within a span of seven residues.

87. (new) A transfection agent according to claim 85 wherein at least two of said plurality of aromatic amino acid residues occur in a pair in the first hydrophobic locus or the second hydrophobic locus.

88. (new) A transfection agent according to claim 86 wherein two or more of said at least two lysine residues are adjacent to one another.
89. (new) A transfection agent according to claim 85 wherein said plurality of aromatic amino acid residues is between three and five aromatic amino acid residues inclusive.
90. (new) A transfection agent according to claim 85 wherein said plurality of aromatic amino acid residues comprises at least two tryptophan residues.
91. (new) A transfection agent according to claim 85 comprising two pairs of aromatic amino acid residues, the first pair being disposed in the first hydrophobic locus and the second pair being disposed in the second hydrophobic locus, and wherein said first and second hydrophobic loci are separated by two amino acids.
92. (new) A transfection agent according to claim 91 wherein said two amino acids separating the first and second hydrophobic loci consist of hydrophilic amino acids.
93. (new) A transfection agent according to claim 92 wherein said hydrophilic amino acids separating the first and second hydrophobic loci are Glu and Thr.
94. (new) A transfection agent according to claim 85 wherein said peptide is a synthetic peptide.
95. (new) A transfection agent according to claim 85 wherein said optional spacer sequence comprises one or more amino acid residues selected from the group consisting of proline, glycine, tyrosine, serine, glutamine, and non-charged amino acids.
96. (new) A transfection agent according to claim 85 wherein said hydrophobic domain comprises a motif (Trp/Tyr)-(Trp/Tyr)-Xaa-Xaa-(Trp/Tyr), wherein the first and second hydrophobic loci are spaced by two amino acids, Xaa-Xaa, wherein each Xaa is a hydrophilic amino acid.

97. (new) A transfection agent according to claim 85 wherein said agent is covalently affixed to a compound selected from the group consisting of a nucleic acid, a peptide, a protein, an antibody, and a derivatives or analog of any of the foregoing.

98. (new) A transfection agent according to claim 85 wherein said agent is non-covalently complexed with a compound selected from the group consisting of a nucleic acid, a peptide, a protein, an antibody, and a derivatives or analog of any of the foregoing.

99. (new) A transfection agent according to claim 85 that further comprises a functional group covalently attached to a terminus of said peptide, wherein the functional group is selected from the group consisting of a cysteamine group, a methyl group, and an alkyl group, and, with respect to the amino terminus of said peptide, an acyl group.

100. (new) A transfection agent according to claim 85 wherein said hydrophilic domain comprises the sequence Lys-Arg-Lys, and wherein said agent further comprises a spacer sequence that comprises at least three amino acid residues of which at least one is a proline or glutamine residue.

101. (new) A transfection agent according to claim 85 that further comprises a functional group to which is covalently conjugated a molecule selected from the group consisting of a stabilizer, a coupler, a dye, a ligand, and an enzymatic substrate.

102. (new) A commercial transfection kit comprising at least one transfection agent according to claim 85 in either aqueous or lyophilized form, said kit further comprising one or more components selected from the group consisting of buffers, positive controls, cells to be transfected, phospholipids, and instructions for use.

103. (new) A pharmaceutical composition comprising a transfection agent according to claim 85.

104. (new) A pharmaceutical composition according to claim 103 wherein said transfection agent is non-covalently complexed with a compound to be delivered to a cell.
105. (new) A pharmaceutical composition according to claim 104 wherein said compound comprises a member selected from the group consisting of a diagnostic compound and a therapeutic compound.
106. (new) A pharmaceutical composition according to claim 104 wherein said compound is a therapeutic compound that is effective to treat one or more afflictions selected from the group consisting of cancer and infectious diseases.
107. (new) A pharmaceutical composition according to claim 104 wherein said compound targets a cell selected from the group consisting of a cancerous cell and a pathogen-infected cell.
108. (new) A pharmaceutical composition according to claim 104 that is effective to transfect cells of interest using molar ratios of agent:compound of between 5:1 and 30:1.
109. (new) A pharmaceutical composition according to claim 104 in aqueous form in which the compound is present at a concentration of between about 0.1  $\mu$ M and about 100  $\mu$ M.
110. (new) A pharmaceutical composition according to claim 104 in aqueous form in which the compound is present at a molar concentration of between about 1  $\mu$ M and about 20  $\mu$ M.
111. (new) A transfection agent comprising a peptide of between about 16 to 30 amino acid residues, said peptide comprising:
- a) a hydrophobic domain comprising at least four amino acid residues, wherein the hydrophobic domain comprises three to five aromatic amino acid residues and a first hydrophobic locus spaced by at least one amino acid residue from a second hydrophobic locus, wherein each of the first and second hydrophobic loci comprise one or more hydrophobic amino acid residues independently selected from the group consisting of Phe, Tyr, Trp, Thr, Met, Leu, Val, Ile, Ala, and His;

- b) a hydrophilic domain comprising up to about twelve amino acid residues, wherein the hydrophilic domain comprises a plurality of basic amino acid residues;
- c) optionally a spacer sequence between said hydrophobic and said hydrophilic domains, wherein said spacer comprises from between one to about ten amino acid residues; and
- d) further optionally a functional group conjugated to one or more termini of said peptide.

112. (new) A transfection agent according to claim 111 wherein said hydrophilic domain is a cation-rich sequence comprised of at least two lysine residues within a span of seven residues.

113. (new) The transfection agent of claim 111 wherein at least two of said plurality of aromatic amino acid residues occur in a pair in the first hydrophobic locus or the second hydrophobic locus.

114. (new) The transfection agent of claim 112 wherein two or more of said at least two lysine residues are adjacent to one another.

115. (new) The transfection agent of claim 111 wherein said plurality of aromatic amino acid residues is between three and five aromatic amino acid residues inclusive.

116. (new) The transfection agent of claim 111 wherein said plurality of aromatic amino acid residues comprises at least two tryptophan residues.

117. (new) The transfection agent of claim 111 comprising two pairs of aromatic amino acid residues, the first pair being disposed in the first hydrophobic locus and the second pair being disposed in the second hydrophobic locus, and wherein said first and second hydrophobic loci are separated by two amino acids.

118. (new) The transfection agent of claim 117 wherein said two amino acids separating the first and second hydrophobic loci consist of hydrophilic amino acids.

119. (new) The transfection agent of claim 118 wherein said hydrophilic amino acids separating the first and second hydrophobic loci are Glu and Thr.
120. (new) A transfection agent according to claim 111 wherein said peptide is a synthetic peptide.
121. (new) A transfection agent according to claim 111 wherein said optional spacer sequence comprises one or more amino acid residues selected from the group consisting of proline, glycine, tyrosine, serine, glutamine, and non-charged amino acids.
122. (new) A transfection agent according to claim 111 wherein said hydrophobic domain comprises a motif (Trp/Tyr)-(Trp/Tyr)-Xaa-Xaa-(Trp/Tyr), wherein the first and second hydrophobic loci are spaced by two amino acids, Xaa-Xaa, wherein each Xaa is a hydrophilic amino acid.
123. (new) A transfection agent according to claim 111 wherein said agent is covalently affixed to a compound selected from the group consisting of a nucleic acid, a peptide, a protein, an antibody, and a derivatives or analog of any of the foregoing.
124. (new) A transfection agent according to claim 111 wherein said agent is non-covalently complexed with a compound selected from the group consisting of a nucleic acid, a peptide, a protein, an antibody, and a derivatives or analog of any of the foregoing.
125. (new) A transfection agent according to claim 111 that further comprises a functional group covalently attached to a terminus of said peptide, wherein the functional group is selected from the group consisting of a cysteamine group, a methyl group, and an alkyl group, and, with respect to the amino terminus of said peptide, an acyl group.
126. (new) A transfection agent according to claim 111 wherein said hydrophilic domain comprises the sequence Lys-Arg-Lys, and wherein said agent further comprises a spacer

sequence that comprises at least three amino acid residues of which at least one is a proline or glutamine residue.

127. (new) A transfection agent according to claim 111 that further comprises a functional group to which is covalently conjugated a molecule selected from the group consisting of a stabilizer, a coupler, a dye, a ligand, and an enzymatic substrate.

128. (new) A commercial transfection kit comprising at least one transfection agent according to claim 111 in either aqueous or lyophilized form, said kit further comprising one or more components selected from the group consisting of buffers, positive controls, cells to be transfected, phospholipids, and instructions for use.

129. (new) A pharmaceutical composition comprising a transfection agent according to claim 111.

130. (new) A pharmaceutical composition according to claim 129 wherein said transfection agent is non-covalently complexed with a compound to be delivered to a cell.

131. (new) A pharmaceutical composition according to claim 130 wherein said compound comprises a member selected from the group consisting of a diagnostic compound and a therapeutic compound.

132. (new) A pharmaceutical composition according to claim 130 wherein said compound is a therapeutic compound that is effective to treat one or more afflictions selected from the group consisting of cancer and infectious diseases.

133. (new) A pharmaceutical composition according to claim 130 wherein said compound targets a cell selected from the group consisting of a cancerous cell and a pathogen-infected cell.

134. (new) A pharmaceutical composition according to claim 130 that is effective to transfect cells of interest using molar ratios of agent:compound of between 5:1 and 30:1.

135. (new) A pharmaceutical composition according to claim 130 in aqueous form in which the compound is present at a concentration of between about 0.1 uM and about 100 uM.

136. (new) A pharmaceutical composition according to claim 130 in aqueous form in which the compound is present at a molar concentration of between about 1 uM and about 20 uM.

137. (new) A transfection agent comprising a peptide of between about 16 to 30 amino acid residues, said peptide comprising:

a) a hydrophobic domain comprising at least four amino acid residues, wherein the hydrophobic domain comprises a plurality of aromatic amino acid residues and a first hydrophobic locus spaced by at least one amino acid residue from a second hydrophobic locus, wherein each of the first and second hydrophobic loci comprise one or more hydrophobic amino acid residues independently selected from the group consisting of Phe, Tyr, Trp, Thr, Met, Leu, Val, Ile, Ala, and His;

b) a hydrophilic domain comprising up to about 12 amino acid residues, wherein the hydrophilic domain comprises a plurality of basic amino acid residues;

c) optionally a spacer sequence between said hydrophobic and said hydrophilic domains, wherein said spacer comprises from between one to about ten amino acid residues; and

d) further optionally a functional group conjugated to one or more termini of said peptide.

138. (new) A transfection agent according to claim 137 wherein said hydrophilic domain is a cation-rich sequence comprised of at least two lysine residues within a span of seven residues.

139. (new) The transfection agent of claim 137 wherein at least two of said plurality of aromatic amino acid residues occur in a pair in the first hydrophobic locus or the second hydrophobic locus.



140. (new) The transfection agent of claim 138 wherein two or more of said at least two lysine residues are adjacent to one another.
141. (new) The transfection agent of claim 137 wherein said plurality of aromatic amino acid residues is between three and five aromatic amino acid residues inclusive.
142. (new) The transfection agent of claim 137 wherein said plurality of aromatic amino acid residues comprises at least two tryptophan residues.
143. (new) The transfection agent of claim 137 comprising two pairs of aromatic amino acid residues, the first pair being disposed in the first hydrophobic locus and the second pair being disposed in the second hydrophobic locus, and wherein said first and second hydrophobic loci are separated by two amino acids.
144. (new) The transfection agent of claim 143 wherein said two amino acids separating the first and second hydrophobic loci consist of hydrophilic amino acids.
145. (new) The transfection agent of claim 144 wherein said hydrophilic amino acids separating the first and second hydrophobic loci are Glu and Thr.
146. (new) A transfection agent according to claim 137 wherein said peptide is a synthetic peptide.
147. (new) A transfection agent according to claim 137 wherein said optional spacer sequence comprises one or more amino acid residues selected from the group consisting of proline, glycine, tyrosine, serine, glutamine, and non-charged amino acids.
148. (new) A transfection agent according to claim 137 wherein said hydrophobic domain comprises a motif (Trp/Tyr)-(Trp/Tyr)-Xaa-Xaa-(Trp/Tyr), wherein the first and second hydrophobic loci are spaced by two amino acids, Xaa-Xaa, wherein each Xaa is a hydrophilic amino acid.

149. (new) A transfection agent according to claim 137 wherein said agent is covalently affixed to a compound selected from the group consisting of a nucleic acid, a peptide, a protein, an antibody, and a derivatives or analog of any of the foregoing.

150. (new) A transfection agent according to claim 137 wherein said agent is non-covalently complexed with a compound selected from the group consisting of a nucleic acid, a peptide, a protein, an antibody, and a derivatives or analog of any of the foregoing.

151. (new) A transfection agent according to claim 137 that further comprises a functional group covalently attached to a terminus of said peptide, wherein the functional group is selected from the group consisting of a cysteamine group, a methyl group, and an alkyl group, and, with respect to the amino terminus of said peptide, an acyl group.

152. (new) A transfection agent according to claim 137 wherein said hydrophilic domain comprises the sequence Lys-Arg-Lys, and wherein said agent further comprises a spacer sequence that comprises at least three amino acid residues of which at least one is a proline or glutamine residue.

153. (new) A transfection agent according to claim 137 that further comprises a functional group to which is covalently conjugated a molecule selected from the group consisting of a stabilizer, a coupler, a dye, a ligand, and an enzymatic substrate.

154. (new) A commercial transfection kit comprising at least one transfection agent according to claim 137 in either aqueous or lyophilized form, said kit further comprising one or more components selected from the group consisting of buffers, positive controls, cells to be transfected, phospholipids, and instructions for use.

155. (new) A pharmaceutical composition comprising a transfection agent according to claim 137.

156. (new) A pharmaceutical composition according to claim 155 wherein said transfection agent is non-covalently complexed with a compound to be delivered to a cell.
157. (new) A pharmaceutical composition according to claim 156 wherein said compound comprises a member selected from the group consisting of a diagnostic compound and a therapeutic compound.
158. (new) A pharmaceutical composition according to claim 156 wherein said compound is a therapeutic compound that is effective to treat one or more afflictions selected from the group consisting of cancer and infectious diseases.
159. (new) A pharmaceutical composition according to claim 156 wherein said compound targets a cell selected from the group consisting of a cancerous cell and a pathogen-infected cell.
160. (new) A pharmaceutical composition according to claim 156 that is effective to transfect cells of interest using molar ratios of agent:compound of between 5:1 and 30:1.
161. (new) A pharmaceutical composition according to claim 156 in aqueous form in which the compound is present at a concentration of between about 0.1  $\mu$ M and about 100  $\mu$ M.
162. (new) A pharmaceutical composition according to claim 156 in aqueous form in which the compound is present at a molar concentration of between about 1  $\mu$ M and about 20  $\mu$ M.
163. (new) A transfection agent comprising a peptide of between about 16 to 30 amino acid residues in length, said peptide comprising:
- a) a hydrophobic domain comprising at least four amino acid residues, wherein the hydrophobic domain comprises a first hydrophobic locus spaced by at least one amino acid residue from a second hydrophobic locus, wherein each of the first and second hydrophobic loci comprise one or more hydrophobic amino acid residues independently selected from the group consisting of Phe, Tyr, Trp, Thr, Met, Leu, Val, Ile, Ala, and His;

- b) a hydrophilic domain comprising up to about 12 amino acid residues, wherein the hydrophilic domain comprises a plurality of basic amino acid residues;
  - c) optionally a spacer sequence between said hydrophobic and said hydrophilic domains, wherein said spacer comprises from between one to about ten amino acid residues; and
  - d) further optionally a functional group conjugated to one or more termini of said peptide,
- wherein the peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO. 1 through 12.

164. (new) A transfection agent according to claim 163 wherein said peptide is a synthetic peptide.

165. (new) A transfection agent according to claim 163 wherein said agent is covalently affixed to a compound selected from the group consisting of a nucleic acid, a peptide, a protein, an antibody, and a derivatives or analog of any of the foregoing.

166. (new) A transfection agent according to claim 163 wherein said agent is non-covalently complexed with a compound selected from the group consisting of a nucleic acid, a peptide, a protein, an antibody, and a derivatives or analog of any of the foregoing.

167. (new) A transfection agent according to claim 163 that further comprises a functional group covalently attached to a terminus of said peptide, wherein the functional group is selected from the group consisting of a cysteamine group, a methyl group, and an alkyl group, and, with respect to the amino terminus of said peptide, an acyl group.

168. (new) A transfection agent according to claim 163 wherein said hydrophilic domain comprises the sequence Lys-Arg-Lys, and wherein said agent further comprises a spacer sequence that comprises at least three amino acid residues of which at least one is a proline or glutamine residue.

169. (new) A transfection agent according to claim 163 that further comprises a functional group to which is covalently conjugated a molecule selected from the group consisting of a stabilizer, a coupler, a dye, a ligand, and an enzymatic substrate.

170. (new) A commercial transfection kit comprising at least one transfection agent according to claim 163 in either aqueous or lyophilized form, said kit further comprising one or more components selected from the group consisting of buffers, positive controls, cells to be transfected, phospholipids, and instructions for use.

171. (new) A pharmaceutical composition comprising a transfection agent according to claim 163.

172. (new) A pharmaceutical composition according to claim 171 wherein said transfection agent is non-covalently complexed with a compound to be delivered to a cell.

173. (new) A pharmaceutical composition according to claim 172 wherein said compound comprises a member selected from the group consisting of a diagnostic compound and a therapeutic compound.

174. (new) A pharmaceutical composition according to claim 172 wherein said compound is a therapeutic compound that is effective to treat one or more afflictions selected from the group consisting of cancer and infectious diseases.

175. (new) A pharmaceutical composition according to claim 172 wherein said compound targets a cell selected from the group consisting of a cancerous cell and a pathogen-infected cell.

176. (new) A pharmaceutical composition according to claim 172 that is effective to transfect cells of interest using molar ratios of agent:compound of between 5:1 and 30:1.

177. (new) A pharmaceutical composition according to claim 172 in aqueous form in which the compound is present at a concentration of between about 0.1  $\mu\text{M}$  and about 100  $\mu\text{M}$ .

178. (new) A pharmaceutical composition according to claim 172 in aqueous form in which the compound is present at a molar concentration of between about 1 uM and about 20 uM.

179. (new) A commercial transfection kit comprising at least one transfection agent comprising a peptide of between about 16 to 30 amino acid residues, said peptide comprising:

a) a hydrophobic domain comprising at least four amino acid residues, wherein the hydrophobic domain comprises a first hydrophobic locus spaced by at least one amino acid residue from a second hydrophobic locus, wherein each of the first and second hydrophobic loci comprise one or more hydrophobic amino acid residues independently selected from the group consisting of Phe, Tyr, Trp, Thr, Met, Leu, Val, Ile, Ala, and His;

b) a hydrophilic domain comprising up to about 12 amino acid residues, wherein the hydrophilic domain comprises a plurality of basic amino acid residues;

c) optionally a spacer sequence between said hydrophobic and said hydrophilic domains, wherein said spacer comprises from between one to about ten amino acid residues; and

d) further optionally a functional group conjugated to one or more termini of said peptide,

wherein the transfection agent is in either aqueous or lyophilized form, and wherein said kit further comprises one or more components selected from the group consisting of buffers, positive controls, cells to be transfected, phospholipids, and instructions for use.

180. (new) A kit according to claim 179 wherein said hydrophilic domain is a cation-rich sequence comprised of at least two lysine residues within a span of seven residues.

181. (new) A kit according to claim 179 wherein at least two of said plurality of aromatic amino acid residues occur in a pair in the first hydrophobic locus or the second hydrophobic locus.

182. (new) A kit according to claim 180 wherein two or more of said at least two lysine residues are adjacent to one another.

183. (new) A kit according to claim 179 wherein said plurality of aromatic amino acid residues is between three and five aromatic amino acid residues inclusive.

184. (new) A kit according to claim 179 wherein said plurality of aromatic amino acid residues comprises at least two tryptophan residues.

185. (new) A kit according to claim 179 comprising two pairs of aromatic amino acid residues, the first pair being disposed in the first hydrophobic locus and the second pair being disposed in the second hydrophobic locus, and wherein said first and second hydrophobic loci are separated by two amino acids.

186. (new) A kit according to claim 185 wherein said two amino acids separating the first and second hydrophobic loci consist of hydrophilic amino acids.

187. (new) A kit according to claim 186 wherein said hydrophilic amino acids separating the first and second hydrophobic loci are Glu and Thr.

188. (new) A kit according to claim 179 wherein said peptide is a synthetic peptide.

189. (new) A kit according to claim 179 wherein said optional spacer sequence comprises one or more amino acid residues selected from the group consisting of proline, glycine, tyrosine, serine, glutamine, and non-charged amino acids.

190. (new) A kit according to claim 179 wherein said hydrophobic domain comprises a motif (Trp/Tyr)-(Trp/Tyr)-Xaa-Xaa-(Trp/Tyr), wherein the first and second hydrophobic loci are spaced by two amino acids, Xaa-Xaa, wherein each Xaa is a hydrophilic amino acid.

191. (new) A kit according to claim 179 wherein said agent is covalently affixed to a compound selected from the group consisting of a nucleic acid, a peptide, a protein, an antibody, and a derivatives or analog of any of the foregoing.

192. (new) A kit according to claim 179 wherein said agent is non-covalently complexed with a compound selected from the group consisting of a nucleic acid, a peptide, a protein, an antibody, and a derivatives or analog of any of the foregoing.

193. (new) A kit according to claim 179 that further comprises a functional group covalently attached to a terminus of said peptide, wherein the functional group is selected from the group consisting of a cysteamine group, a methyl group, and an alkyl group, and, with respect to the amino terminus of said peptide, an acyl group.

194. (new) A kit according to claim 179 wherein said hydrophilic domain comprises the sequence Lys-Arg-Lys, and wherein said agent further comprises a spacer sequence that comprises at least three amino acid residues of which at least one is a proline or glutamine residue.

195. (new) A kit according to claim 179 that further comprises a functional group to which is covalently conjugated a molecule selected from the group consisting of a stabilizer, a coupler, a dye, a ligand, and an enzymatic substrate.

196. (new) A kit according to claim 179 wherein the transfection agent is formulated as a pharmaceutical composition.

197. (new) A kit according to claim 196 wherein said transfection agent is non-covalently complexed with a compound to be delivered to a cell.

198. (new) A kit according to claim 197 wherein said compound comprises a member selected from the group consisting of a diagnostic compound and a therapeutic compound.

199. (new) A kit according to claim 197 wherein said compound is a therapeutic compound that is effective to treat one or more afflictions selected from the group consisting of cancer and infectious diseases.



200. (new) A kit according to claim 197 wherein said compound targets a cell selected from the group consisting of a cancerous cell and a pathogen-infected cell.

201. (new) A kit according to claim 197 wherein said compound is effective to transfect cells of interest using molar ratios of agent:compound of between 5:1 and 30:1.

202. (new) A kit according to claim 197 wherein said composition is in aqueous form and the compound is present at a concentration of between about 0.1  $\mu\text{M}$  and about 100  $\mu\text{M}$ .

203. (new) A kit according to claim 197 wherein said composition is in aqueous form and the compound is present at a molar concentration of between about 1  $\mu\text{M}$  and about 20  $\mu\text{M}$ .